enrolled into the ACOS-Registry (Acute Coronary Syndrome, 154 hospitals) in Germany. We analysed the prospective data of STEMI-pts with special respect to the smoking status.

Results: Out of 5122 consecutive pts with STEMI, 1852 (36%) were current smokers and 2753 (54%) had never smoked (nonsmokers). Smokers were at mean 15 years younger, more often male and had less often hypertension and diabetes as additional cardiovascular risk factors. Smokers did receive acute reperfusion therapy more often. The hospital mortality in nonsmokers was three times higher than in smokers. After correcting for differences in baseline characteristics and acute reperfusion and adjunctive therapy in a multivariate analysis smoking did not influence hospital mortality after STEMI (OR 0.80, 95% CI 0.60-1.06).

Conclusion: In smokers STEMI occurred 15 years earlier in age than in nonsmokers. In a multivariate analysis smoking did not influence the outcome of STEMI.

Parameter	Smokers n=1852	Nonsmokers n=2753	p-value
Age (years)	56	71	<0.01
Male gender	81.6 %	60.4 %	<0.01
Prior MI	8.4 %	12.8 %	<0.01
Hypercholesteremia	47.4 %	40.2 %	<0.01
Hypertension	45.0 %	63.3 %	<0.01
Diabetes	16.1 %	30.5 %	<0.01
CK max (U/l)	625	532	<0.01
Acute Reperfusion	78.7 %	64.8 %	<0.01
Thrombolysis	26.7 %	20.7 %	<0.01
Primary PCI	52.0 %	44.1 %	<0.01
Hospital Mortality	4.7 %	13.3 %	<0.01

8:45 a.m.

869-2 Comparison of the Importance of Increasing Pathogen Burden, Elevated C-Reactive Protein, and the Presence of Antibodies to Heat Shock Protein 60 on Myocardial Infarction or Death

Jianhui Zhu, Stephen E. Epstein, Joseph B. Muhlestein, Javier F. Nieto, Amy Wasserman, Benjamin D. Horne, David Rott, Jeffrey L. Anderson, Washington Hospital Center, Washington, DC, LDS Hospital, Salt Lake City, UT

In addition to the importance of traditional risk factors, recent evidence suggests that infectious pathogens, C-reactive protein (CRP) and heat shock protein (HSP) play roles in the progression of atherosclerosis and can be used as outcome predictors. In the present study, we compared the relative importance of a) pathogen burden (seropositivity to cytomegalovirus, hepatitis A virus, C. pneumoniae, H. pylori, herpes simplex virus type 1 and type 2), b) CRP levels, and c) anti-human HSP60 antibodies in predicting myocardial infarction (MI) or death. The patient cohort consisted of 890 patients (77% men, mean age 65 years) with coronary artery disease (CAD) documented by coronary angiography ($\geq$ 70% stenosis). The mean follow-up period was 3 years. By both univariate and Cox multivariate regression analyses, pathogen burden and elevated CRP levels were strong and independent predictors of incident MI or death. The highest relative hazard was conveyed by pathogen burden (Table 1). In contrast, HSP60 antibodies were not significant determinants of MI or death. We conclude that in patients with documented CAD, both pathogen burden and elevated CRP levels are important independent predictors of MI or death, suggesting that infection and inflammation contribute to the disease processes leading to acute coronary occlusion. Although HSP60 has been associated with angiographic evidence of the presence and extent of CAD, it's role in the acute complications of CAD is still to be determined.

Table 1. Comparison of Relative Hazard (95%CL) of Incident MI or Death

	Unadjusted	Adjusted For CAD Risk Factors
Pathogen Burden0-3	1.0	1.0
4	1.9 (0.8-4.4)	1.5 (0.6-3.5)
5	3.2 (1.4-6.9)	2.6 (1.2-5.7)
6	4.6 (2.1-9.9)	3.1 (1.4-6.8)
CRP Tertile 1	1.0	1.0
2	1.9 (1.3-2.9)	1.8 (1.2-2.6)
3	1.9 (1.3-2.9)	1.7 (1.1-2.5)
HSP60 Ab (+)	1.0	1.0
HSP60 Ab (-)	1.2 (0.8-1.6)	1.2 (0.8-1.6)

9:00 a.m.

869-3 Increased Concentrations of Bone Marrow-Derived Stem Cells in Peripheral Blood After Acute Myocardial Infarction

Antonio Maria Leone, Sergio Rutella, Felicita Andreotti, Luca Pierelli, Mariaelena Lombardi, Giuseppe Leone, Filippo Crea, Università Cattolica del Sacro Cuore, Rome, Italy

Background: recent studies in experimental models have shown that bone marrow-derived stem cells (BMSCs) can regenerate myocardial tissue after a myocardial infarction. Moreover, the presence of cardiomyocytes of extracardiac origin has been reported in human transplanted hearts. It is reasonable to assume, therefore, that BMSCs may be released into the peripheral blood after an acute myocardial infarction (AMI), migrate towards the heart, and there differentiate into cardiomyocytes to repair, at least in part, the damaged tissue. The aim of this study was to evaluate whether BMSC concentrations increase in peripheral blood after an AMI. **Methods:** BMSC concentrations were measured by flow-cytometry as CD34+ cells/microliter (mcl) in the peripheral blood of 22 patients with AMI after 1, 3, 5 and 7 days from the event and in 11 healthy controls without cardiovascular risk factors, of similar age, sex and race. **Results:** In agreement with the literature, the median concentration of CD34+ cells in healthy controls was <1/mcl (0.47/mcl, interquartile range - IR - 0 to 0.94). In contrast, in the absence of clinical and laboratory findings of hemoconcentration, the median concentration of CD34+ cells in patients with AMI was significantly increased at 1, 3, 5 and 7 days from the event to 4.46/mcl (IR 2.6 to 8.4, p=0.0005), 2.91/mcl (IR 2.16 to 4.045, p=0.0014), 5.03/mcl (IR 2.38 to 7.9, p=0.0013), and 7.925 (IR 5.26 to 12.68, p=0.0075), respectively (Figure). **Conclusions:** In patients with AMI there is an increase in peripheral bone marrow-derived stem cell concentrations. These results support the hypothesis that these cells may migrate, differentiate, proliferate and contribute to remodel the infarcted myocardium.

9:15 a.m.

869-4 Association of Left Ventricular Hypertrophy Regression and Heart Rate Reduction With Determinants of Myocardial Oxygen Consumption and Cardiovascular Events: The LIFE Study

Richard B. Devereux, Kristian Wachtell, Eva Gerdts, Peter Aurup, Kurt Boman, Jonathan Edelman, Markku Nieminen, Vasilios Papademetriou, Ying Wan, Bjorn Dahlof, Stevo Julius, Weill Cornell Medical Center, New York, NY

Background: Experimental studies have demonstrated that increased myocardial O2 consumption demand due to left ventricular hypertrophy (LVH) increases the likelihood and size of myocardial infarction (MI) with a standardized coronary occulusion, but no human data exist to separate the potentially beneficial effects of LVH regression and reduced myocardial O2 demand on the rate of MI in treated hypertensive patients. Methods: In a double-blind, randomized, parallel-group design 960 participants in the Losartan Intervention for Endpoint reduction in hypertension (LIFE) study (average age 66 years, blood pressure 174/98 mmHg) and ECG-documented LVH were assigned once daily losartan- or atenolol-based therapy and underwent echocardiography after 1,2,3,4 and 5 years' treatment. LV mass and the LV mass x end-systolic stress x heart rate triple product were measured as indices of LVH and O2 demand. Results: Blood pressure was reduced similarly in the two treatment arms (mean=-29.7/16.2 versus -28.0/16.0 mmHg, NS) but heart rate fell more on atenolol (mean=-7.2 versus -1.1 beats per minute, p<0.001). LV mass was reduced more in losartan than atenolol-treated patients (mean=-22.0 versus -17.7 g/m2, p=0.021). In contrast, the triple product fell more on atenolol-based therapy (mean=-28% versus -18%, p<0.001). In Cox regressions adjusting for treatment, baseline LV mass index and baseline and in-treatment pressures, each 25 g/m2 lower LV mass index was associated with risk reductions (95% CI) of 22 (5-34, p=0.02)% for stroke and 33 (17-43, p=0.001)% for cardiovascular (CV) mortality but only 13 (33 t0 -17, NS)% for MI. Conclusion: Losartan-based antihypertensive therapy reduced LV mass more but atenolol reduced the triple product (index of myocardial O2 demand) by 10% more, potentially contributing to less reduction in MI than stroke or CV death associated with reduction of LV mass and to less effect of losartan than atenolol on MI than stroke or CV death in the entire LIFE study.

9:30 a.m.

869-5 The Assessment of Myocardial Viability With Delayed Contrast Enhancement Using Computed Tomography

Aaron So, Jennifer Hadway, Jane Sykes, Gerald Wisenberg, Frank Prato, Tin-Su Pan, Ting-Yim Lee, Lawson Health Research Institute and Robarts Research Institute, London, ON, Canada, General Electric Medical Systems, Waukesha, WI

Background: Delayed enhancement of contrast has emerged as the most popular MRI approach to detect ischemic injury to myocardium. We have developed a CT technique for the quantitative measurement of myocardial distribution volume (MDV) of contrast media using retrospective ECG gated cine scanning.

Methods: Four 15-25 kg beagles were used for the study. For MDV measurement, a 30 s baseline (without contrast) cine scan was performed in synchrony with ECG recording using a General Electric Medical Systems (GEMS) LightSpeed multi-slice CT scanner. Contrast (Omnipaque, 225 mgI/ml) was then constantly infused for 30-60 min before the scan was repeated. Images were reconstructed with half-scan data (330 ms) at 0.1 s interval and those at end-diastole (ED) were selected with SmartScore (GEMS) and averaged with CT Perfusion 2 (GEMS). MDV maps were generated by subtracting the averaged non-contrast enhanced ED images from the corresponding averaged constant infusion images. The difference images were normalized to the enhancement in the

aorta. Baseline measurements of MDV were obtained on each beagle prior to 2 hours occlusion of the left anterior descending artery (LAD) and then repeated at 4 hours reperfusion and also at day 4, 9, 16, 23 and 30 post. At day 30 post, the heart was removed following MDV measurement and scanned ex-vivo at high spatial resolution before it was sliced and stained with TTC.

Results: MDV in the apical region of the heart increased from a mean baseline value of 0.4 ± 0.1 ml/g to 0.9 ± 0.05 ml/g immediately after reperfusion and remained above 0.6 ml/g until day 4 post. From day 9 post MDV normalized except for a thin subendocardial rim in the apical region. High resolution ex-vivo scan of the removed heart confirmed the location of the rim enhancement seen in the MDV image to be subendocardial. TTC staining further confirmed that the rim enhancement was infarcted tissue. MDV in normal myocardium at the lateral free wall of the left ventricle was 0.4 ± 0.05 ml/g at all time points.

Conclusion: We concluded from our preliminary results that ECG- gated contrast-enhanced CT scanning is a promising and simple approach for studying myocardial damage from ischemia and its resolution with time.

9:45 a.m.

869-6 **Can Anatomic No-Reflow Be Prevented by Pharmacologic Treatment With Adenosine and Verapamil?**

Thorsten Reffelmann, Robert A. Kloner, The Heart Institute, Good Samaritan Hospital, University of Southern California, Los Angeles, CA

Objectives: The aim was to investigate the effects of intravenous adenosine and verapamil on anatomic no-reflow (ANR) in a rabbit model of coronary artery occlusion and reperfusion.

Background: Verapamil and adenosine have been successfully used in treatment of clinical no-reflow after direct angioplasty for acute myocardial infarction. However, whether these agents reduce anatomic no-reflow associated with myocardial necrosis, as it occurs in animal models of coronary occlusion and reperfusion, is unknown.

Methods: ANR (thioflavin S at end of reperfusion), regional myocardial blood flow (RMBF, radioactive microspheres), and infarct size (IS, triphenyltetrazolium) were compared in anesthetized, open-chest rabbits (ischemia-reperfusion: 30-120 minutes) receiving intravenous adenosine at reperfusion (875 µg/kg bolus, then 175 µg/kg/min until the end of reperfusion) against controls (saline) (n=8, each), and rabbits treated with intravenous verapamil at reperfusion (50 µg/kg bolus, then 150 µg/kg/h) against saline (n=8, each).

Results: Both regimes significantly lowered systolic and diastolic blood pressure, reduced specific vascular resistance in the risk area (RA)(adenosine: -38.7% and -38.7% at 30 and 120 min of reperfusion, verapamil: -52.5% and -54.3% at 30 and 120 min of reperfusion), and verapamil increased RMBF within the risk area (verapamil: 48±7%, saline: 33±5% of non-ischemic flow at 120 min of reperfusion). IS (adenosine: 34.1±4.3%, saline: 39.6±6.2% of RA) and ANR (adenosine: 28.8±3.2%, saline: 35.2±5.8% of RA) were not significantly different in the adenosine protocol, and significantly correlated with each other (r=0.98). Similarly, verapamil did not result in significant effects on IS (verapamil: 42.2±5.9%, saline: 38±6.3% of RA), and ANR (verapamil: 37.6±5.5%, saline: 34.9±5.7% of RA), which again showed a significant correlation (r=0.96). ANCOVA analysis revealed that neither treatment uncoupled ANR from IS.

Conclusion: Despite reducing vascular resistance within the RA, both adenosine and verapamil at reperfusion did not reduce ANR, suggesting that vasospasm is not a major contributor to anatomic perfusion defects in this experimental model.

ORAL CONTRIBUTIONS

872 The Old and the New: The ECG and Novel Biomarkers in Acute Coronary Syndromes

Wednesday, April 02, 2003, 8:30 a.m.-10:00 a.m.
McCormick Place, Room S404

8:30 a.m.

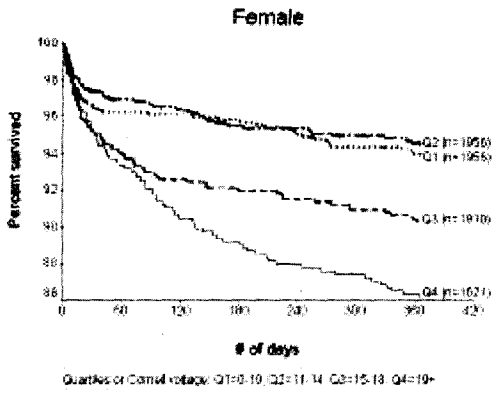
872-1 **Does the Presence of Electrocardiographic Left Ventricular Hypertrophy Predict One-Year Mortality in Non-ST Elevation Acute Coronary Syndromes?**

Michael S. Lauer, Yuling Fu, Wei-Ching Chang, Robert M. Califf, Maarten Simoons, Lars Wallentin, Eric J. Topol, Paul W. Armstrong, Cleveland Clinic Foundation, Cleveland, OH, University of Alberta, Edmonton, Canada

Background: Whereas electrocardiographic (ECG) left ventricular hypertrophy (LVH) predicts long-term mortality in otherwise healthy people, its importance as a predictor of death in the setting of NSTEMI acute coronary syndromes (ACS) is not known.

Methods: Patients with ACS who were enrolled in the GUSTO IV randomized trial had baseline ECGs read in a blinded core laboratory. LV mass was assessed by Cornell voltage, which is the sum of the amplitude of the S wave in V3 and the R wave in lead V1. LVH was defined as a voltage ≥ 28 mm in men and ≥ 20 mm in women.

Results: Baseline ECG data were available in 7443 (95%) of 7800 patients enrolled. ECG LVH was present in 747 patients (10%). During follow-up, 260 patients (3.5%) died by 30 days and 574 (7.7%) by 1 year. ECG LVH tended to predict death at 30 days (4.4% vs. 3.4%, P=0.14), while it was associated with death at one year (12.2% vs. 7.2%, odds ratio = 1.76, 95% CI 1.41 to 2.26, P < 0.0001). There was increased risk of death with increasing Cornell voltage, especially in women. (Figure)



After adjusting for age, ST-segment depression, troponin, C reactive protein, and other confounders using logistic regression, Cornell voltage remained independently predictive of 1-year mortality (p=0.018), but only in women (p=0.031 for the interaction between Cornell voltage and sex; in gender specific analyses, p=0.005 and 0.339 for Cornell voltage in women and men, respectively).

Conclusion: ECG LVH at baseline is an independent predictor of 1year mortality among women presenting with ACS.

8:45 a.m.

872-2 **The Prognostic Value of ST-Segment Elevation in Lead AVR in Patients With a First Acute Myocardial Infarction Without Other ST Elevation**

José A. Barrabés Jaume Figueras, Cristina Moure, Josefa Cortadellas, Jordi Soler-Soler, Hospital Universitari Vall d'Hebron, Barcelona, Spain

Background: ST segment elevation (STE) in lead aVR has been associated with severe coronary lesions in patients with acute coronary syndromes, but the prognostic significance of this finding is unknown.

Methods: We analyzed the initial ECG in 775 consecutive patients admitted to our center with a first acute myocardial infarction without STE in leads other than aVR.

Results: Compared to the remaining patients, those with STE in lead aVR had a higher baseline risk profile and a more frequent and extensive ST segment depression in other leads. The rates of death and other in-hospital complications were strongly associated with the magnitude of STE in lead aVR, while CK-MB levels were not (Table). After adjustment for age, Killip class and presence and location of ST segment depression, the odds ratios for death in the last two groups shown in the table were, respectively, 5.6 (95% confidence interval, 2.0-15.5) and 7.8 (3.1-19.9). Among 437 patients catheterized within six months, those with STE in lead aVR had a lower left ventricular ejection fraction and a more extensive coronary artery disease.

Conclusion: Lead aVR contains important prognostic information in patients with a first acute myocardial infarction without other STE. As the worse outcome predicted by STE in lead aVR appears to be related to a more severe coronary artery disease, an early invasive approach might be especially beneficial in these patients.

	No STE in lead aVR (n=525)	STE 0.05-0.1 mV in lead aVR (n=116)	STE >=0.1 mV in lead aVR (n=134)	P value
Death, %	1.3	8.6	19.4	<0.001
Reinfarction, %	2.1	6.0	6.0	0.009
Angina, %	10.3	19.8	26.9	<0.001
Heart failure, %	3.2	10.3	30.6	<0.001
CK-MB peak, IU/l	127±103	128±102	119±95	NS
Left ventricular ejection fraction, %	66±12	63±11	59±16	<0.001
Left main or three vessel disease, %	22.0	42.6	66.3	<0.001